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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/420,433	10/12/1999	DAVID SIDRANSKY	JHU1180-1	2810

7590 03/26/2007

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/420,433	SIDRANSKY, DAVID	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-12,14,18-22 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-12,14,18-22 and 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL ACTION

1. This action is responsive to the Amendment filed May 8, 2006 and the complying complete set of claims filed December 12, 2006. Claims 1, 12, 14, 18-20 and 25 have been amended, and claims 13 and 28-31 have been canceled. Claims 1-4, 7-12, 14, 18-22, and 24-26 are now pending and under consideration. Applicant's amendments and arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and/or objections not reiterated in this action have been withdrawn. **This action is FINAL.**

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

3. In view of the cancellation of claims 28-31, the rejections of those claims under 35 USC 112, first and second paragraphs, set forth in the Office action of January 6, 2006 are moot.

4. In view of the amendment of claims 1, 20, and 25 to delete the language "does not exhibit microscopic characteristics indicative of neoplastic pathology," the rejections of those claims and the claims dependent therefrom under 35 USC 112, first and second paragraphs, set forth in the Office action of January 6, 2006 are moot.

5. In view of the cancellation of claim 13, the rejection of the claim under 35 USC 112, first paragraph for lack of enablement set forth in the Office action of January 6, 2006 is moot.

6. Claims 1-4, 7-12, 14, 18-22, and 24-26 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for the reasons set forth in the Office action of January 6, 2006. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is noted that while the claims have been amended to recite the terminology "histologically normal" in lieu of the limitation "does not exhibit microscopic characteristics indicative of neoplastic pathology," the claims as amended continue to lack enablement for the reasons that were given in the Office action of January 6, 2006.

The response traverses the rejection on the following grounds.

First, the response argues that the claimed invention "is not 'completely unpredictable,'" as the specification describes adjacent surgical margins and distant tissues that appear "'normal' when examined by standard histopathological methods, and further describes standard procedures that may be used to examine such samples. This argument has been thoroughly considered but is not persuasive. The examiner has not alleged that analysis of "histologically normal" surgical margins and distant tissues cannot be conducted, or that such analyses *per se* require undue experimentation. Rather, as discussed in the Office action of January 6, 2006, the claims lack enablement because applicant has not provided evidence that mutated versions of the particular nucleic acids set forth in the claims may actually be detected in such specimens. It is as a result of this absence of evidence, both in view of the specification and the prior art, that the claims lack enablement.

Next, the response argues that p53 is exemplary of the nucleic acids that are actually set forth in applicant's claims. However, the data in the specification is limited to detection of a single gene, p53, in surgical margins and lymph nodes in patients afflicted with head and neck squamous cell carcinoma (i.e., a single type of cancer). The specification provides no actual evidence that these findings extend to any other gene or any other cancer type, and applicant has not, e.g., provided any further documentation or evidence in support of these assertions. Further, as noted in the Office action of January 6, 2006, the prior art as exemplified by Neri et al indicates that it is unknown what genes other than p53 might be detectable in specimens that appear normal by histological analysis. Thus, applicant's arguments are not persuasive.

Finally, the response argues that applicant has provided sufficient guidance to enable the practice of the claimed invention without undue experimentation. However, applicant again relies on the teachings in the specification with regard to how specimen types may be analyzed, referring to Examples 2 and 4. The examiner has not alleged that analysis of such specimen types cannot be conducted without undue experimentation; rather, the claims lack enablement because it has not been established that nucleic acids meeting the requirements of the claims may actually be detected in specimens at a point in time when those specimens still appear "histologically normal."

This rejection is maintained.

THE FOLLOWING ARE NEW GROUNDS OF REJECTION NECESSITATED BY APPLICANT'S AMENDMENTS:

7. Claims 1-4, 7-12, 14, 18-22 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-4 and 7-11 are indefinite over the recitation of the phrase "extracting the nucleic acid present in the neoplasm, wherein the nucleic acid is selected from APC, DCC, NF1, NF2, RET, VHL, and WT-1." This language is confusing because the phrase "extracting the nucleic acid present in the neoplasm" suggest that one is to extract any nucleic acid present in the neoplasm; however, the language "wherein the nucleic acid is selected from" appears to require, e.g., extraction of only a particular target molecule. Further, in the phrase "detecting the nucleic acid in the neoplasm and in histologically normal tissue specimen," it is not clear whether "the nucleic acid" refers to the previously recited nucleic acid "present in the neoplasm" or to the particular target molecule. Finally, it is not clear how the recited "histologically normal tissue specimen" relates to the previously mentioned "tumor margin tissue specimen," and while the claim recites an objective of detecting a "mammalian mutant target nucleic acid in a neoplasm and in a tumor margin tissue specimen," the final step of the claims not refer to detection of a "mutant target nucleic acid" or otherwise indicate how this objective is achieved. Clarification is required.

Claims 2, 3, and 11 are indefinite because claim 2 refers to a step of "detecting the presence of the mutant target nucleic acid;" however, claim 1 as amended no longer includes such a step. Thus, the manner in which the claims further limit claim 1 is not clear.

Claims 12 and 14 are indefinite over the recitation of the limitation "selected from at least APC, DCC, NF1, NF2, RET, VHL, and WT-1." The terminology "at least" renders the claims unclear because it appears to suggest that one might select something other than one of the nucleic acids listed, while the recitation "selected from.... APC, DCC, NF1, NF2, RET, VHL, and WT-1," in contrast, suggests that one must select a nucleic acid from those listed (and if no such selection is required, the inclusion of the list in the claim is non-limiting and meaningless). Clarification is required.

Claim 18 is indefinite over the recitation of the limitation "the target mutant neoplastic nucleic acid" because there is insufficient antecedent basis for the limitation in the claim.

Claim 19 is indefinite over the recitation of the new limitation "isolating a tissue specimen wherein the tissue specimen appears histologically normal" because there is no indicate as to how this method steps relates to other method steps of the claim.

Claim 19 is indefinite over the recitation of the limitation "the target mutant neoplastic nucleic acid" because there is insufficient antecedent basis for the limitation in the claim.

Claims 20-22 and 24 are indefinite because claim 20 has been amended such that it appears to require multiple tissue specimens, and it is unclear which specimen constitutes "the tissue specimen" of the detecting step. Further, it is not clear how the "isolating" step relates to the claimed method, which includes a prior step of extracting nucleic acid "in the tissue specimen."

Claim Rejections - 35 USC § 102

8. In view of the cancellation of claims 28-30, the rejection of those claims under 35 USC 102(a) set forth in the Office action of January 6, 2006 is moot.

Claim Rejections - 35 USC § 103

9. In view of the cancellation of claims 13 and 31, the rejections of those claims under 35 USC 103(a) set forth in the Office action of January 6, 2006 are moot.

10. In view of the amendments to claims 12 and 18-19, such that the claims now require the detection of mutated forms of the recited nucleic acids in tissue specimens having a histologically normal appearance, the rejections of the claims under 35 USC 103(a) set forth in the Office action of January 6, 2006 are withdrawn.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634